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News Release

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VA scientists discover promising alternative to morphine

By Tyler Grimes

Scientists from the Southeast Louisiana Veterans Health Care System partnered with Tulane University School of Medicine to develop a new drug alternative to traditional painkillers like morphine, but with fewer side effects and less potential for addiction.

The research study, funded primarily by Department of Veterans Affairs, builds on a discovery in 1997 by Dr. James Zadina, SLVHCS Senior Research Career Scientist, and his team.

They found a peptide, a small protein found in the brain, called endomorphin that acts on the same receptor to relieve pain in the body as morphine.

Since that discovery, Zadina's team has tested many engineered versions of the peptide structure with three goals: to make it stable so it could serve as a drug, to provide long-lasting pain relief and to avoid side effects.

"Being a very different structure than morphine, which comes from a plant, we thought our peptide might be better at relieving pain with fewer side effects because it is similar to the peptide naturally found in the brain," Zadina said.

To explore their theory, Zadina's team conducted several tests in rats and mice, the most commonly used animal models that predict effects in humans. The first tests determined variations of the drug that produced effective pain relief, reduced respiratory depression, and had less impairment on motor coordination.

"In an overdose, it's the respiratory depression that kills you, so reducing this effect would be critical for making it a safer drug," he said.

According to the World Health Organization, approximately 69,000 deaths are caused by opioid overdose worldwide each year, with more than 28,000 of those in the United States.

Another of his team's experiments examined the rats' motor coordination by observing their ability to run on a wheel. The rats given the new drug were able to keep pace and stay on the wheel much longer than those given morphine.

"Older adults are the most in need of pain relief, while at the same time they are at the greatest risk of suffering severe injury due to a fall," he said.

Another situation where loss of motor coordination is dangerous is in military settings such as the battlefield. In these cases, effective pain relief without motor impairment is a critical safety issue.

The research also showed that the new drug produces less tolerance than morphine. Tolerance is the need for increased doses over time to maintain the same pain-relieving effect, which, in turn, can also increase chances of other side effects, Zadina said.

The new drug does not require as much of a dose increase as morphine. This difference may be due to a nervous system inflammatory response that was seen with morphine but not the endomorphin-based drug, according to Zadina. The absence of an inflammatory effect may also indicate improved pain treatment for conditions like traumatic brain injury, where inflammation in the brain can contribute to long-term cognitive impairments.

Finally, the investigators tested several animal models for reward and addiction potential. They discovered that animals given morphine were more likely to return to the place where they were given morphine and also were more willing to work harder at pressing a bar for a morphine infusion.

These same behaviors were not observed with the new endomorphin-based drug.

Tests in rats have been shown to be highly predictive of outcomes in humans, and indicate that the new drug is unlikely to be abused or addictive, explained Zadina.

“Most currently used opioid painkillers, like oxycodone and hydrocodone, are based on chemicals that were discovered around 100 years ago, or morphine, discovered about 200 years ago, and these start from chemicals from the opium plant,” he said. “It’s been the same few chemicals, just with different formulas. To get different results, our thinking is why not start from scratch with a new compound.”

Zadina said he believes that his compound could show fewer side effects, not cause a pro-inflammatory response, and be less addictive because it is based on a chemical found naturally throughout the body in the same areas as opioid receptors.

Zadina’s team hopes the drug will address two major issues for Veterans-- better treatment for pain and reduced opioid addiction.

According to a 2014 study by the U.S. Department of Health and Human Services National Center for Complementary and Integrative Health, 44 percent of active duty service members suffer from chronic pain and about 15 percent reported opioid use after completing a combat deployment.

“The (Veteran) population is different from the civilian population,” said Dr. Sanjay Sharma, SLVHCS Pain Management anesthesiologist. “The Veterans are subject to more chronic pain and comorbidities like PTSD, traumatic brain injury, anxiety and depression, make them more vulnerable to addiction and tolerance.”

According to Sharma, many Veterans are on opioids for chronic pain and face an inherent risk of death as well as several severe side effects. He said he is hopeful about the potential of Zadina’s research and what it could mean for patients.

“They are doing a great favor to not only the Veterans but the entire community of patients who have chronic pain,” Sharma said. “If all the clinical trials are successful, we will have a drug that will have minimal adverse effects like addiction potential, tolerance and respiratory depression while retaining the strong pain relieving properties.”

There is still a lot of work to do before human clinical trials can begin, including safety, toxicology and pharmacology tests. Zadina said that he is very grateful for the support of VA in his team’s ongoing research.

“The VA has been there since the beginning, and this project is of utmost importance to our patients - I’m excited to be part of that,” he said.

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